Abstract 293

TITLE: Rates and Determinants of Positive HIV Screening Test Results in Uninfected Participants in Phase I/II Trials of Candidate HIV-1 Vaccines

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BACKGROUND/OBJECTIVES: The AIDS Vaccine Evaluation Group has carried out over 30 phase I/II trials in which 2750 uninfected volunteers have been enrolled using over 20 different vaccine candidates. Many vaccine approaches have induced antibodies in recipients that can be detected by commercially available HIV test kits. However, the rate of positive serologic responses in these trials is dependent on both the kit used for determination of the antibody response and the type of vaccine immunogen employed in the trial.

METHODS: Most of the vaccine trials have utilized either recombinant gp160, gp120, vaccinia or canarypox vectors encoding HIV-1 genes, or combinations of these immunogens. At the end of study a commercially available ELISA and WB is routinely performed. These tests are also often carried out at peak titer, which is usually 2 weeks after the third or fourth immunization. Positive ELISA tests or the possibility of intercurrent infection are evaluated by an algorithm which incorporates both serologic and nucleic acid based tests for final infection determination.

RESULTS: HIV serology at final visit (= 6 months after last immunization)

Immunization	**Abbott EIA N (%)**	**Western blot N (%)**	**Positive for EIA and WB N (%)**
Control	2/252 (0.8%)	5/225 (2.2%)	1/253 (0.4%)
gp160	71/131 (54.2%)	94/129 (72.9%)	68/130 (52.3%)
gp120	20/438 (4.6%)	118/380 (31.1%)	15/424 (3.4%)
vaccinia ± gp120 or gp160	68/169 (40.2%)	106/156 (68.4%)	64/169 (37.9%)
canarypox ± gp120	9/101 (8.9%)	13/111 (11.7%)	3/111 (2.7%)

In more recent trials of canarypox constructs encoding mutiple genes plus subunit boosts, the rates of false positive results at peak titers by the Abbott EIA has been 73%, whereas the Sanofi kit that does not incorporate a p24 antigen has a positive rate of 1.3%. In addition, we have reported volunteers who have been falsely diagnosed as infected by outside evaluators who did not take into account the vaccine-induced responses.

CONCLUSIONS: Distinguishing infection versus vaccine-induced antibodies is an important consideration in the design of present and future candidate vaccines. The greatest problems for diagnosis will arise in vaccine candidates that include the gp41 immunodominant determinant or in test kits that continue to use p24 antigens, as many approaches are likely to include the gag gene. The use of gp120 alone leads to few problems in testing if appropriate kits are utilized and a reliance on Western blot is decreased. Such results emphasize the need to continue public discussion on this topic in view of ongoing/ planned Phase III trials.

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